AMENDMENTS TO THE SPECIFICATION

Please replace the title with the following:

REGULATION OF LUNG TISSUE BY ~~HEDGEHOG-LIKE POLYPEPTIDES~~ PATCHED THERAPEUTICS AND FORMULATIONS AND USES RELATED THERETO

On page 1, please replace the second paragraph with the following amended paragraph:

RELATED APPLICATIONS

This application is a continuation of U.S. Patent Application Serial No. 09/394,020, filed on September 10, 1999, now abandoned, which claims priority to U.S. Provisional Patent Application Serial No. 60/099,952, filed September 11, 1998, the specifications of each of which are incorporated by reference herein in their entirety.

Please replace the paragraph bridging pages 8-9 with the following amended paragraph:

FIG. 1. Morphology and epithelial phenotype of Shh -/- mouse lungs. (~~a~~A) At 12.5 dpc, the wt mouse lung has branched several times to give rise to distinct lobes (arrows). (~~b~~B) Trachea and esophagus are separate tubes. (~~c~~C) Cross-section at the level of the lung shows branching and lobation. (~~d~~D) At 12.5 dpc, Shh-deficient lungs have failed to undergo lobation or subsequent extensive branching. (~~e~~E) Trachea and esophagus remain fused at the tracheoesophageal septum. (~~f~~F) Mutant lungs have branched only once. (~~g~~G) At 18.5 dpc, airsac formation is in progress in the wt and the respiratory surface is in tight association with blood vessels. (~~h~~H) There is little branching or growth of the poorly vascularized mutant lungs, but airsac formation at the distal epithelial tips is apparent (arrows). (~~i~~I) By 18.5 dpc, wild-type lungs have established the conducting airways and respiratory bronchioles, alveolar formation is in progress. (~~j~~J) In contrast, in a mutant lung of the same stage, branching is dramatically decreased. Only a few primary branches (arrows) and air sacs (arrowheads) are present. (~~k~~K) In the wild-type, trachea and esophagus are separated. The trachea is lined by columnar cells, the esophagus by stratified epithelium. (~~l~~L) Air sacs are made of cuboidal cells. (~~m~~M) In the mutant, trachea and esophagus are fused to form a fistula. Differentiation into columnar and stratified epithelium is apparent, (~~n~~N) as is the characteristic cuboidal epithelium of the air sacs. Demarcation lines between terminal bronchioles

and respiratory surface are indicated. (~~o~~O) Proximal lung epithelium of the 18.5 dpc wt lung expresses CCSP in Clara cells, and (~~p~~P) SP-C in type II pneumocytes of the distal epithelium. (~~q~~Q) CCSP and (~~p~~R) SP-C are expressed in the correct proximo-distal domain in the mutant. Bars denote 1 mm (~~g,h~~ G, H only) or 10 μm. (~~a,d,g,h~~A, D, G, H) are ventral views, all others transverse sections. Abbreviations: t--trachea, e--esophagus, l--lung, h--heart, s--stomach, mb--mainstem bronchus, b--bronchus, tb--terminal bronchiole, a--air sac.

Please replace the first complete paragraph on page 9 with the following amended paragraph:

FIG. 2. In situ analysis of gene expression in the lungs of Shh mutants. Expression of the genes indicated was investigated in whole mount vibratome sections through lungs removed from wt 11.5 (left panel) and 12.5 dpc (center panel), and Shh-mutant 12.5 dpc (right panel) embryos. Figures 2A to 2K each shows the expression of: (A) Ptc-1; (B) Pct-2; (C) Gli-1; (D) Gli-2; (E) Gli-2; (F) Bmp-4; (G) Wnt-7b; (H) Wnt-2; (I) FGF-R2; (J) FGF-10; and (K) Nkx-2.1.